## **CLAIMS**

1. A polymeric delivery system for sustained release administration of a quinazolinone derivative of formula (I)

5 wherein: n=1-2

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R<sub>1</sub> which may be the same or different at each occurrence is a member of the group consisting of hydrogen, halogen, nitro, benzo, lower alkyl, phenyl and lower alkoxy;

R<sub>2</sub> is a member of the group consisting of hydroxy, acetoxy and lower alkoxy;

R<sub>3</sub> is a member of the group consisting of hydrogen and lower alkenoxy-carbonyl; and pharmaceutically acceptable salts thereof,

wherein the quinazolinone is released at a therapeutically effective dose for a period of at least one month.

- 15 2. The polymeric delivery system of claim 1 wherein the delivery system is formulated for local administration or topical administration to a target site in a subject.
  - 3. The delivery system of claim 2, wherein the route of administration is selected from implantation, subcutaneous injection or deposition within a body cavity.
  - 4. The delivery system of claim 1, wherein the quinazolinone derivative of formula (I) is halofuginone.
  - 5. The delivery system of claim 3, wherein the delivery system is formulated as an implant other than as a coating for a stent.
- 25 6. A polymeric delivery system for sustained release of a quinazolinone derivative of formula (I):

wherein: n=1-2

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R<sub>2</sub> is a member of the group consisting of hydroxy, acetoxy and lower alkoxy;

R<sub>3</sub> is a member of the group consisting of hydrogen and lower alkenoxy-carbonyl; and pharmaceutically acceptable salts thereof;

the polymeric delivery system comprising biocompatible two-phase polymeric beads comprising a core compartment comprising a water-in-oil emulsion surrounded by a polymeric shell compartment comprising a biocompatible polymer, wherein the discontinuous aqueous phase of the core compartment of the polymeric beads comprises the quinazolinone derivative of formula (I).

- 7. The delivery system of claim 6, wherein the biocompatible polymer is a natural or synthetic hydrophilic polymer.
- 8. The delivery system of claim 7, wherein the biocompatible hydrophilic polymer is a polysaccharide or a protein.
- 9. The delivery system of claim 8, wherein the polysaccharide is selected from: alginate, dextran, cellulose, cellulose derivatives, dextran sulfate, chondroitin sulfate, heparan sulfate, heparin, keratan sulfate, dermatan sulfate, and algal polyglycan sulfates.
  - 10. The delivery system of claim 9, wherein the polysaccharide polymer is alginate.
  - 11. The delivery system of claim 8, wherein the protein is selected from: gelatin, collagen, elastin, fibrin and albumin.

- 12. The delivery system of claim 11, wherein the protein is gelatin.
- 13. The delivery system of claim 6, wherein the quinazolinone derivative of formula (I) is halofuginone.
- 14. The delivery system of claim 6, wherein the quinazolinone derivative of formula (I) is released at a therapeutically effective concentration for a time period ranging from a several days to a several months.
- 15. The delivery system of claim 6, wherein the delivery system is formulated for local administration or topical administration to a target site.
- 16. The delivery system of claim 15, wherein the route of administration is selected from implantation, subcutaneous injection or deposition within a body cavity
- 17. The delivery system of claim 6, wherein the polymeric beads are dispersed within an oil-based formulation or water-based selected from an oily suspension, emulsion, cream and gel.
- 18. A polymeric delivery system for local sustained release of a quinazolinone derivative of formula (I):

$$R^{1}_{n} \longrightarrow N \longrightarrow R_{2}/n_{n} \longrightarrow N \longrightarrow N$$

$$R_{3}$$

$$R_{3}$$

$$R_{3}$$

wherein: n=1-2

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R<sub>1</sub> which may be the same or different at each occurrence is a member of the group consisting of hydrogen, halogen, nitro, benzo, lower alkyl, phenyl and lower alkoxy;

R<sub>2</sub> is a member of the group consisting of hydroxy, acetoxy and lower alkoxy;

R<sub>3</sub> is a member of the group consisting of hydrogen and lower alkenoxy-carbonyl; and pharmaceutically acceptable salts thereof;

the polymeric delivery system comprising a biocompatible polymeric film wherein the quinazolinone derivative of formula (I) is homogeneously dispersed within the film.

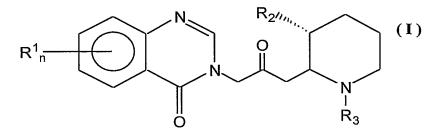
- 19. The delivery system of claim 18, wherein the biocompatible polymer is a selected from a synthetic biodegradable and a synthetic non-biodegradable polymer.
- 20. The delivery system of claim 19, wherein the synthetic polymer is selected from: polyacrylic acid polymers, polylactic acid polymers, polycaprolactone polymers, polyglycolic acid and various copolymers thereof.
- 10 21. The delivery system of claim 20, wherein the synthetic biocompatible polymer is polycaprolactone.

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- 22. The delivery system of claim 18, wherein the polymeric film is a coating of an article.
- 23. The delivery system of claim 18, wherein the quinazolinone derivative of formula (I) is halofuginone.
- 24. The delivery system of claim 18, wherein the quinazolinone derivative of formula (I) is released at a therapeutically effective concentration for a time period ranging from a several days to a several months.
- 25. The delivery system of claim 18, wherein the delivery system is suitable for a route of administration selected from subcutaneous implantation and deposition within a body cavity.
- 26. The delivery system of claim 18, wherein the delivery system is suitable for application topically at a target site of a subject.
- 27. A polymeric delivery system for sustained release of a quinazolinone derivative of formula (I)



wherein: n=1-2

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 $R_1$  which may be the same or different at each occurrence is a member of the group consisting of hydrogen, halogen, nitro, benzo, lower alkyl, phenyl and lower alkoxy;

R<sub>2</sub> is a member of the group consisting of hydroxy, acetoxy and lower alkoxy;

R<sub>3</sub> is a member of the group consisting of hydrogen and lower alkenoxy-carbonyl; and pharmaceutically acceptable salts thereof;

the delivery system comprising a polymeric complex comprising at least one type of biocompatible negatively-charged polymeric molecule conjugated through electrostatic interactions to the quinazolinone derivative of formula (I), said quinazolinone derivative of formula (I) having a positive charge at physiological pH.

- 28. The delivery system of claim 27, wherein the negatively charged biocompatible polymer is a synthetic or natural biocompatible polymer.
- 29. The delivery system of claim 28, wherein the synthetic or natural polymer is selected from polyacrylic acid polymers, alginate polymers, polylactic acid polymers, polyglycolic acid and various copolymers thereof.
- 30. The delivery system of claim 29, wherein the negatively charged biocompatible polymer is alginate or polyacrylic acid.
- 31. The delivery system of claim 27, wherein the quinazolinone derivative of formula (I) is halofuginone.
- 32. The delivery system of claim 27, wherein the quinazolinone derivative of formula (I) is released at a therapeutically effective concentration for a time period ranging from a several days to a several months.
- 33. The delivery system of claim 27, wherein the delivery system is suitable for a route of administration selected from subcutaneous implantation and deposition within a body cavity.
- 34. The delivery system of claim 27, wherein the delivery system is suitable for application topically at a target site of a subject.

35. A polymeric delivery system for sustained release of a quinazolinone derivative of formula (I):

$$R^{1} \xrightarrow{N} \xrightarrow{R_{2}/n_{n_{1}}} (I)$$

wherein: n=1-2

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R<sub>1</sub> which may be the same or different at each occurrence is a member of the group consisting of hydrogen, halogen, nitro, benzo, lower alkyl, phenyl and lower alkoxy;

R<sub>2</sub> is a member of the group consisting of hydroxy, acetoxy and lower alkoxy;

R<sub>3</sub> is a member of the group consisting of hydrogen and lower alkenoxy-carbonyl; and pharmaceutically acceptable salts thereof,

the polymeric delivery system comprises biocompatible polymeric beads in suspension, wherein the polymeric beads comprise the quinazolinone derivative of formula (I).

- 36. The delivery system of claim 35, wherein the biocompatible polymer is a natural or synthetic hydrophilic polymer.
- 37. The delivery system of claim 36, wherein the biocompatible natural polymer is selected from a polysaccharide and a protein.
- 38. The delivery system of claim 37, wherein the polysaccharide is selected from: alginate, dextran, cellulose, cellulose derivatives, dextran sulfate, chondroitin sulfate, heparan sulfate, heparan, keratan sulfate, dermatan sulfate, and algal polyglycan sulfates.
  - 39. The delivery system of claim 38, wherein the polysaccharide polymer is alginate.
  - 40. The delivery system of claim 37, wherein the protein is selected from: gelatin, collagen, elastin, fibrin and albumin.

41. The delivery system of claim 40, wherein the protein is gelatin.

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- 42. The delivery system of claim 35, wherein the quinazolinone derivative of formula (I) is halofuginone.
- 43. The delivery system of claim 35, wherein the quinazolinone derivative of formula (I) is released at a therapeutically effective concentration for a time period ranging from a several days to a several months.
- 44. The delivery system of claim 35, wherein the delivery system is suitable for a route of administration selected from implantation, subcutaneous injection and deposition within a body cavity.
- 10 45. The delivery system of claim 35, wherein the delivery system is formulated for topical administration to a target site in a subject.
  - 46. The delivery system of claim 35, wherein the polymeric beads are dispersed within an oil-based or water-based formulation selected from an oily suspension, emulsion, cream or gel.
- 47. A method of preparing the biocompatible polymeric beads of claim 6 comprising:
  - a. mixing an aqueous suspension of the quinazolinone derivative of formula
    (I) in an oily phase to form a water-in-oil emulsion;
  - b. homogenizing the mixture of step (a);
  - c. applying a polymeric shell around small droplets of the emulsion by means of core/shell extrusion, and
  - d. solidifying the shell to form two phase core-and-shell-structured polymeric beads.
  - 48. A method of preparing the polymeric film of claim 18 comprising:
    - a. dissolving the quinazolinone derivative of formula (I) in an organic solvent to form a drug solution;
    - b. mixing the polymer in suitable solvent to form a polymeric solution;
    - c. mixing the drug solution with the polymeric solution; and
    - d. evaporating the polymer solvent to form the polymeric films comprising said quinazolinone derivative of formula (I) homogenously dispersed therein.

49. A method of preparing the biocompatible delivery system of claim 27 comprising:

- a. dissolving the quinazolinone derivative of formula (I) in an aqueous phase to form a drug solution;
- b. mixing the polymer in suitable aqueous phase to form a polymeric solution;
- c. mixing the drug solution with the polymeric solution for sufficient time to form polymeric complexes; and
- d. precipitating the polymeric complexes.

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- 50. A method of preparing the biocompatible delivery system of claim 35 comprising:
  - a. suspending the quinazolinone derivative of formula (I) in an aqueous solution to form a drug suspension;
  - b. mixing the polymer in suitable solvent to form a polymeric solution;
  - c. mixing the polymeric solution with a cross linking agent and the drug suspension to form polymeric beads comprising said quinazolinone derivative of formula (I).
  - 51. A method of delivering a stable therapeutic concentration of the quinazolinone derivative of formula (I), comprising: administering to a subject in need thereof the biocompatible polymeric delivery system according to claim 6, wherein said delivery system continuously delivers a stable therapeutic concentration of said quinazolinone derivative of formula (I) for a period of time ranging from days to months.
  - 52. The method of claim 51 wherein the quinazolinone derivative of formula (I) is halofuginone.
  - 53. A method of treating or inhibiting a disease selected from a neoplastic disease, restenosis, a disease associated with angiogenesis and a disease associated with fibrosis, comprising administering to a subject in need thereof a quinazolinone derivative of formula (I) in a biocompatible polymeric delivery system according to claim 6, the delivery system continuously delivering a stable therapeutic concentration of the

quinazolinone derivative for a period of time ranging from days to months, thereby treating the disease.

- 54. The method of claim 53 wherein the quinazolinone derivative of formula (I) is halofuginone.
- 55. A method of delivering a stable and local therapeutic concentration of a quinazolinone derivative of formula (I), comprising: administering to a subject in need thereof the biocompatible polymeric delivery system according to claim 18, wherein the delivery system continuously delivers a stable therapeutic concentration of the quinazolinone derivative of formula (I) for a period of time ranging from days to months.
  - 56. The method of claim 55 wherein the quinazolinone derivative of formula (I) is halofuginone.
  - 57. A method of treating or inhibiting a disease selected from a neoplastic disease, restenosis, a disease associated with angiogenesis and a disease associated with fibrosis comprising administering to a subject in need thereof a quinazolinone derivative of formula (I) in a biocompatible polymeric delivery system according to claim 18, the delivery system continuously delivering a stable therapeutic concentration of the quinazolinone derivative for a period of time ranging from days to months, thereby treating the disease.

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- 58. The method of claim 57 wherein the quinazolinone derivative of formula (I) is halofuginone.
- 59. A method of delivering a stable and local therapeutic concentration of the quinazolinone derivative of formula (I) comprising: administering to a subject in need thereof the biocompatible polymeric delivery system according to claim 27, wherein the delivery system continuously delivers a stable therapeutic concentration of said quinazolinone derivative of formula (I) for a period of time ranging from days to months.
- 60. The method of claim 59 wherein the quinazolinone derivative of formula (I) is halofuginone.

61. A method of treating or inhibiting a disease selected from a neoplastic disease, restenosis, a disease associated with angiogenesis and a disease associated with fibrosis comprising administering to a subject in need thereof a quinazolinone derivative of formula (I) in a biocompatible polymeric delivery system according to claim 27, wherein the delivery system continuously delivers a stable therapeutic concentration of the quinazolinone derivative for a period of time ranging from days to months, thereby treating the disease.

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- 62. The method of claim 61 wherein the quinazolinone derivative of formula (I) is halofuginone.
- 63. A method of delivering a stable and local therapeutic concentration of the quinazolinone derivative of formula (I) comprising: administering to a subject in need thereof the biocompatible polymeric delivery system according to claim 35, wherein the delivery system continuously delivers a stable therapeutic concentration of the quinazolinone derivative of formula (I) for a period of time ranging from days to months.
- 64. The method of claim 63 wherein the quinazolinone derivative of formula (I) is halofuginone.
- 65. A method of treating or inhibiting a disease selected from a neoplastic disease, restenosis, a disease associated with angiogenesis and a disease associated with fibrosis comprising administering to a subject in need thereof a quinazolinone derivative of formula (I) in the biocompatible polymeric delivery system of claim 35, wherein said delivery system continuously delivers a stable therapeutic concentration of halofuginone for a period of time ranging from days to months, thereby treating the disease.
- 66. The method of claim 65 wherein the quinazolinone derivative of formula (I) is halofuginone.
- 67. An implant comprising the polymeric delivery system of claim 6.
- 68. An implant comprising the polymeric delivery system of claim 18.
- 69. An implant comprising the polymeric delivery system of claim 27.
  - 70. An implant comprising the polymeric delivery system of claim 35.